

Claims

1. A recombinant DNA sequence encoding an analog of mammalian FGF.

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2. The DNA sequence of claim 1 which encodes a human FGF protein analog.

3. The DNA sequence of claim 2 which encodes a 10 human basic FGF protein analog.

4. The DNA sequence of claim 3 which encodes a human basic FGF protein analog with reduced affinity for heparin binding.

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5. The DNA sequence of claim 4 encoding a human basic FGF protein analog, comprising substituting one or more positively charged amino acid residues located in a heparin binding domain encompassing residues 128 through 20 138 with a neutral or negatively charged amino acid.

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6. The DNA sequence of claim 5 wherein the neutral or negatively charged amino acid is selected from the group consisting of serine, threonine or glutamic acid.

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7. The DNA sequence of claim 5 wherein the location and composition of the substituted amino acid is selected from the group consisting of serine<sub>128</sub>, glutamic acid<sub>128</sub>, threonine<sub>129</sub>, serine<sub>128</sub>/threonine<sub>129</sub>, and serine<sub>138</sub>.

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8. The DNA sequence of claim 2 which encodes a human basic FGF protein analog wherein one or more cysteine residues are replaced by a neutral amino acid and said protein analog exhibits the biological activity of 5 native basic FGF.

9. The DNA sequence of claim 8 wherein the neutral amino acid is serine or alanine.

10 10. The DNA sequence of claim 9 wherein the substituted cysteine residue is at position 78, 96 or a combination thereof.

15 11. The DNA sequence of claim 5 which encodes a human basic FGF protein analog wherein said analog binds to a receptor for FGF and has reduced ability to induce a biological response.

20 12. The DNA sequence of claim 3 which encodes an amino-terminal deletion analog of FGF having FGF antagonist activity.

25 13. The DNA sequence of claim 12 wherein said deletion spans residues 1 through 24 of human basic FGF.

14. The DNA sequence of claim 12 encoding a human basic FGF analog further comprising one or more positively charged amino acid residues located in a heparin binding domain encompassing residues 128 through 30 138 substituted with a neutral or negatively charged amino acid.

15. The DNA sequence of claim 3 which is operably linked to control sequences for expression.

16. The DNA sequence of claim 15 wherein the control sequences include a transcription termination signal.

5 17. The DNA sequence of claim 3 which is transformed into a recombinant host cell.

10 18. A recombinant vector containing the DNA sequence of claim 3 and effective in expressing FGF or an analog thereof.

15 19. The vector of claim 18 which is selected from the group consisting of plasmids pUC9-TSF11 and pUC9delH3-pTSF-3.

20 20. The vector of claim 18 wherein the DNA sequence encoding an FGF analog is operably linked to control sequences compatible with bacteria.

25 21. The vector of claim 18 wherein the DNA sequence encoding an FGF analog is operably linked to control sequences compatible with mammalian hosts.

25 22. Recombinant host cells transformed with the vector of claim 18.

23. Bacterial cells transformed with the vector of claim 20.

30 24. Mammalian cells transformed with the vector of claim 21.

35 25. A method for producing FGF protein analogs which comprises culturing host cells harboring the DNA of claim 3 and recovering the FGF protein analog.

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26. The method of claim 25 wherein the host cells are bacterial.

27. The method of claim 25 wherein the host 5 cells are mammalian.

28. A human basic FGF protein analog having reduced affinity for heparin binding comprising substituting one or more positively charged amino acid residues 10 located in a heparin binding domain encompassing residues 128 through 138 with a neutral or negatively charged amino acid.

29. A human basic FGF protein analog wherein 15 the cysteine at positions 78, 96, or a combination thereof, is replaced by a neutral amino acid and said analog exhibits the biological activity of native, human basic FGF.

30. The human basic FGF protein analog of claim 29 which is bFGF-C78/96S.

31. An antagonist of human basic FGF.

32. The FGF antagonist of claim 31 wherein the first 24 amino terminal residues of basic FGF are deleted.

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